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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,437	08/15/2005	Giorgio Casari	1069-PCT-US	7476

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,437	CASARI ET AL.	
	Examiner	Art Unit	
	STEVEN H. STANDLEY	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV, claims 14-15, in the reply filed on 2/06/08 is acknowledged. The traversal is on the ground(s) that the other groups share a special technical feature with the elected group. This is not found persuasive because the examiner has determined that the claims do not make a contribution over the prior art. Therefore the claims lack a special technical feature that defines a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Sequence Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and /or amino acid sequences set forth in 37 CFR 1821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because 37 CFR 1.821 (a)(2)(c-d) states that each sequence disclosed must appear separately in the sequence listing and in the text of the description and claims whenever described. For example, a SEQ ID NO: and sequence listing is required for the sequences shown in Figures 1 and 2, the oligonucleotide pairs shown on page 3-4, 8-9, and 14. See also pages 3-4 of the specification. Applicant may bring the figure(s) into compliance by amending either the figure(s) or the "Brief Description of the Drawings" to recite the appropriate sequence identifier. See MPEP 2422 & 2431.

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Applicant must comply with the requirements of the sequence rules (37 CFR 1.821-1.825). Note that failure to respond to both the requirements for sequence compliance and the Office action below will be held as nonresponsive, and may result in abandonment of this application.

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Information Disclosure Statement

3. Reference #6 has been considered. However, in the absence of a submitted sequence with a SEQ ID NO, the relevance of the references cannot be assessed by the examiner.

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4. The listing of references in the specification on page 15 and 16 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Note that 37 CFR 1.98.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 14-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identification of an agonist or antagonist agent that comprises: i) transfection of a cell line with a recombinant DNA sequence encoding the polypeptide of ATP1A2, exposure of said transfected cells to a test agent, and measurement of Na,K atpase activity with labeled ions, does not reasonably provide enablement for a method of identifying a functional portion or a gene-regulating portion of the subunit, nor is it enabled for a generic mutant resistant to ouabain, nor is it enabled for use of an agent to treat a transgenic animal in a method of identification of an antagonist, nor is it enabled for mutant forms of the atpase expressed in eukaryotic or prokaryotic cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

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The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method directed at doing two separate and distinct things that require different steps. However, the steps recited would not teach one skilled in the art how to accomplish at least one aspect of the preamble. Secondly, the nature of the invention is a method of identifying agonists and antagonists to a molecule that is essentially structureless, since a generic mutant of a protein can be anything. The nature of the invention is also a method wherein a "gene" is transfected. However, the genomic structure is not taught in the specification or the prior art. Thus, the invention transfects an unknown structure.

The state of the prior art is that the gemonic structure of ATP1A2 is not known and only a limited number of mutants of ATP1A2 are known, and those mutants affect function and sensitivity to ouabain. Therefore one would not know how to make and use all mutants that are resistant to ouabain or who to make or use a generic gene of ATP1A12. The working examples appear to support mutation at a single locus in the ATP1A polypeptide. Therefore the specification lacks guidance or example for the recitation of "a mutant isoform" and "a gene."

The breadth of the claims for variants and genes in claims 14 and 15 are such that the transfected variant could be anything at all. All the protein must be is insensitive to ouabain.

Therefore, one of skill in the art would not know how to make or use the invention commensurate with the scope of the claims without undue experimentation because the nature of the invention is complex and contradictory, one cannot reasonably identify a

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structurally unknown molecule using a structurally unknown protein, the art provides no support, and the breadth of the claims encompasse everything.

6. Claims 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods involving transfection of a "gene" for a "mutant isoform" of ATP1A2. The claims do not require that the, gene, recombinant dna, or polypeptide possess any particular biological activity except the negative limitation of ouabain insensitivity, nor any particular conserved structure, or other disclosed distinguishing feature. Therefore, there are no clear structural limitations on the complex of genes, nucleic acids and polypeptides claimed in the method. Thus, the claims are drawn to a genus of genes, nucleic acids and polypeptides that constitute a collection of molecules that is completely undefined.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. In the instant application, no such distinctions have been identified. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is

a partial structure in the form of a recitation of a name. There is not even identification of any particular portion of the structure that must be conserved.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

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Therefore, only nucleic acids encoding the amino acid sequence set forth in a SEQ ID NO: of ATP1A2, versus the full breadth currently claimed, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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7. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is a method of identification of an agonist or antagonist agent of the ATP1A2 or a functional portion or a gene-regulating portion of the subunit. However, the subsequent steps are not directed at identification of a functional portion or a gene-regulating portion of the subunit. They are directed at identifying an agonist or antagonist.

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8. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is a method of identification of an agonist or antagonist agent of the ATP1A2 or a functional portion that comprises the phases: I) use of the agent to treat a

transgenic animal that expresses a mutant isoform of NaKpump, and ii) use of the agent to treat equkaryotc or prokaryotic cell lines that express mutant or normal forms of the ATP1A2. However, the steps accomplish neither of the methods identified in the preamble.

9. Claims 14-15 lack a step wherein the objective of the method is completed.

Claims14-15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a step in which the objective of the method is accomplished.

10. Claim 15 recites the limitation "use of the agent" in i) and ii). There is insufficient antecedent basis for this limitation in the claim. The method is a method to identify an agent. The agent is not identified in the claims. The subsequent steps assume the agent has been identified.

Claim 15 provides for the use of an agent to treat a transgenic, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

11. Claim 15 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966),

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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12. Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Asano et al. (1997).

Asano et al. teach a method of identification of an agonist (SCH28080) of human "ATPase" by transfection of HEK cells with a gene (without introns) of a mutant form of the ATPase (which is a rabbit alpha subunit of a H+, K+ ATPase; see Experimental Procedures) that is resistant to ouabain (see top of abstract); Asano et al teaches appropriate exposure to the agent (see figure 2, pg 17670); Asano et al teaches measurement of activity in relation to ion transport with labeled ions (see atpase activity assay, page 17669). Therefore Asano et al. meet all the limitations of claim 14.

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13. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Golovina et al. (2002).

Golovina et al teach a method of identification of an agonist or antagonist agent comprising the use of the agent (CPA and/or ouabain; see abstract) to treat a transgenic animal that expresses a mutant isoform of Na ATPase which is deleted (see "knock out mice" page C476). Thus, Golovina et al meets all the limitations of claim 15.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Stucker can be reached on **(571) 272-0911**.

The fax number for the organization where this application or proceeding is assigned is **(571) 273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
3/11/08

/Robert C. Hayes, Ph.D./
Primary Examiner, Art Unit 1649